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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,524	12/18/2001	Patrick D. Kilgannon	27866/34162A	8164

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,524	KILGANNON ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-27* is/are pending in the application.

4a) Of the above claim(s) *18-22* is/are withdrawn from consideration.

5)☒ Claim(s) *23-26* is/are allowed.

6)☒ Claim(s) *27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 3-12-04 has been entered into the record. Claims 1-17 have been cancelled. Claims 18-27 are pending. Claims 23-27 are under examination. Claims 18-22 are withdrawn from consideration.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Election/Restrictions

This application contains claims 18-22 drawn to an invention nonelected without articulated traverse in the paper filed 7-21-03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejections Withdrawn

The rejection of claim 27 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of US Patent No. 5,773,293 is withdrawn in view of the properly filed terminal disclaimer.

The rejection of claims 23-26 under 35 USC 112, first paragraph is withdrawn in view of the declaration filed 3-12-04.

The rejection of claim 27 under 35 USC 112, second paragraph is withdrawn in view of Applicants amendment to the claim.

The rejection of claim 27 under 35 USC 102(b) as anticipated by Bailly et al is withdrawn in view of Applicants amendment to the claim.

The rejection of claim 27 under 35 USC 102(b) as being anticipated by Oka et al (Neuroscience 35:93-103, 1990) in light of Yoshihara et al (Neuron 12:541-544, 1994) is withdrawn in view of Applicants arguments and in view of the lack of any evidence of

record that establishes that the monoclonal antibody binds SEQ ID NO:28 or a fragment thereof or human variant thereof.

Rejections Maintained

The rejection of claim 27 under 35 USC 112, first paragraph as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for reasons made of record in the office action mailed 11-18-03.

Applicants argue that it is well known what is meant in the art by referring to antibody binding specificity and that Applicants previously referred to Harlow et al "Antibodies: A Laboratory Guide, " (1988) to obtain their definition of specific binding. Applicants stated previously that Harlow sets out that a specifically binding antibody is one that only recognizes the appropriate antigen and has a defined unique specificity. This is not persuasive. This again states that the monoclonal antibody has to exclusively bind the appropriate antigen. Applicants have not provided for such or tested for such. This definition is not in the specification as filed. Further, a defined unique specificity does not mean that the antibody is not cross-react. As shown by the art previously provided by the examiner, while each monoclonal antibodies have a defined unique specificity to an epitope based on their specific gene structure, it does not mean that they do not specifically bind antigens that share the specific epitopic structure. As such, although each monoclonal antibody has a unique epitopic specificity, it will bind any molecule possessing the unique epitope defined by the monoclonal antibody. Binding of the monoclonal antibody is specific for its epitope. Applicants miss the concept, a single monoclonal antibody binds a single epitope and therein lies the specificity. A monoclonal antibody is specific for an epitope. It is not specific for an antigen. Applicants do not

conceive of a monoclonal antibody that has exclusive binding. Applicants argue that Harlow et al defines that the specificity of the immune response is controlled by a simple mechanism, that one cell recognizes one antigen". This is not persuasive, the principal set forTH is not that the recognition is exclusive of all other antigens, but that each cell has one receptor that binds a single epitope on an antigen. This is represented by the entire sentence in context "- because all of the antigen receptors on a single lymphocyte are identical." Therefore in context, this discusses the nature of the specificity of a single cell for a single epitope, not one monoclonal antibody exclusively binds a single antigen. Harlow et al teaches that any molecule that can bind to an antibody is an antigen. Harlow et al does not teach that a single cell can not bind different antigens with the same epitope. The concept of epitopes is clearly set forth in Harlow et al, in page 23-24. Applicants argue that the specification defines specific at page 8, lines 2-5. This is not persuasive, it is not an exclusive definition. The claims does not clearly exclude all other monoclonal antibodies that bind an epitope in common with another antigen sharing that same epitope. Further, the examiner maintains that cross-reactive antibodies are indeed recognized by the art as specifically binding their epitope. Therefore, one of skill in the art would not recognize specific binding or specific immunoreacting as exclusive to all other antigens as argued by Applicants.

The rejection is maintained for reasons made of record.

The rejection of claim 27 under 35 USC 102(b) as being unpatentable over Oka et al (Neurosciene 35:93-103, 1990) in view of Goding et al (Monoclonal Antibodies, 1983 Academic Press Inc, pages 56-97) and in light of Yoshihara et al (Neuron 12:541-544, 1994) is maintained for reasons made of record in the office action mailed 11-18-03.

Applicants' arguments have been carefully considered but are not persuasive. Applicants argue that it would not be expected that humans have orthologs of telencephalin/ICAM-4 would exist. This is not persuasive, ICAM-1, ICAM-2 and ICAM-3

all have orthologs in mammalian systems. There is full reason to expect that telencephalin/ICAM-4 would also have an ortholog in human. Applicants argue that since the monoclonal antibody failed to cross-react with other species that Oka et al teach that there is no reason to expect that orthologs exist. This is not persuasive, because in the next sentence Oka et al teach that "However, using polyclonal antibody against the purified telencephalon-specific antigen, we were able to examine immunohistochemically the brains of various mammalian species." These studies using the polyclonal antibody clearly demonstrate orthologs in every mammalian species tested. As such, the lack of binding of the monoclonal antibody does not teach away from the combination because it was not used in the combination, the polyclonal antibody was relied upon. Further, Applicants argue that one skilled in the art would have no reasonable expectation of success at isolating the molecule of SEQ ID NO:27 and 28. This is not persuasive the claims are not so limited and include fragments of SEQ ID NO:27 and 28 that are as small as a single epitope (6 consecutive amino acids) and the claims clearly encompass variants and fragments of variants (see markush member (c)).

The rejection is therefore maintained.

New Rejections Based on Amendment

Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

All of the referenced passages discuss ICAM-4 in general, as is clearly intended to encompass more than human subgenus of ICAM-4 and specifically references "rat". ICAM-4 is not defined in the specification as limited to human. The claim is drawn to monoclonal antibodies that bind fragments of human or hybridizing variants of ICAM-4

and Applicants point to page 6, lines 9-13 and page 7, lines 18-21 for support. The discussions recited do not support the now claimed subject matter to *monoclonal antibodies* that bind the subgenus of human ICAM-4 fragments and hybridizing variants as claimed. Further, page 7, lines 4-5 describe cells as antigens not fragments or antibodies binding fragments. Applicants point to the specification at page 37, lines 5-7 for support for monoclonal antibodies that bind human ICAM-4 hybridizing variants. This is not persuasive, this passage discusses gene identity and does not convey conception in the written description of hybridizing variants nor antibodies that bind such. Further, the recitation of the subgenus of hybridizing human variants is not, and can not be supported by the relied upon the rat ortholog of page 37, line 5-7.

Claim 27 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification discloses SEQ ID NO: 27 which corresponds to the cDNA sequence encoding the human ICAM-4 protein represented by SEQ ID NO:28. SEQ ID NO: 27 encoding the human ICAM-4 protein meets the written description provision of 35 USC 112, first paragraph. However, claim 27 is directed to encompass human ICAM-4 hybridizing variants and fragments thereof which encompass mutated sequences, allelic variants and splice variants and so forth. None of these human protein variant sequences or fragments thereof meet the written description provision of 35 USC 112, first paragraph, because the specification fails to provide either sufficient written description of human protein alleles, variants, mutants and fails to provide sufficient written description support for hybridizing variants. As such, the single human ICAM-4 polypeptide of SEQ ID NO:28 encoded by the single human ICAM-4 nucleic acid of SEQ

ID NO:27 provides insufficient written description to support the genus of antibodies binding human ICAM-4 fragments, human ICAM-4 variants and fragments thereof encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 28, the skilled artisan cannot envision the detailed chemical structure of the encompassed human ICAM-4 proteins, regardless of the complexity or simplicity of the method of isolation and can not envision antibodies specific for such. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. In the instant case the specification similarly lacks written description for the human subgenus of hybridizing variants and fragments thereof. Because, the specification lack written description for hybridizing nucleic acid variants, human ICAM-4 polypeptide variants encoded thereby or fragments thereof, they similarly lack written description for the now claimed monoclonal antibodies that specifically immunoreact therewith. The species of monoclonal antibody specifically disclosed as binding to SEQ ID NO:28 are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Status of Claims

Claims 23-26 are allowed. Claim 27 stands rejected. Claims 18-22 are withdrawn from consideration.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-

0855. The examiner can normally be reached on M-F 6:30 pm - 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patricia A. Duffy

Primary Examiner

Art Unit 1645